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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/505,244

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Scott K. Kuwada

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02/03/2009

Ballard Spahr Andrews & Ingersoll, LLP

SUITE 1000

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ATLANTA, GA 30309-3915

EXAMINER

PAGONAKIS, ANNA

ART UNIT

PAPER NUMBER

1614

MAIL DATE

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02/03/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/505,244

**Applicant(s)**

KUWADA, SCOTT K.

**Examiner**

ANNA PAGONAKIS

**Art Unit**

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 8-21, 26-28, 37-42, 53-57 and 65-72 is/are pending in the application.
- 4a) Of the above claim(s) 16, 17, 19, 20 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 8-15, 18, 21, 26-32, 34-40, 42, 53-57, 64-72 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 1 sheet, 11/14/2008
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

Applicant's amendment filed 11/14/2008 has been received and entered into the present application.

Claims 1, 8-21, 26-28, 37-42, 53-57, 65-72 are currently pending. Accordingly, claims 1, 37-40, 65-72 are currently amended and claims 2-7, 22-25, 29-36, 43-52, 58-64 have been cancelled. Claims 16-17, 19-20 and 41 remain withdrawn from consideration.

As reflected by the attached, completed copy form PTO/SB/08 (one page total), the Examiner has considered the cited references.

Applicant's arguments, filed 11/14/2008 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, 65, 67-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 indicates that NFkappaB inhibitor is administered to a subject that "has had" (past tense) a tumor resected. Claims 65, 67-72 make no sense to me in view of the past tense of the independent claim. The administration is to someone who had already had a tumor resected. Therefore claims that provide administration before resection can not properly limit the independent claim.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 8-15, 18, 21, 26-28, 37-40, 42, 53-57, 64-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Izban et al. (Human Pathology, Vol. 31, No. 12, 2000) and Khan et al (US 7,175,679).

Izban et al. teach the use of the elected compound, BAY 11-7085 for its use as a NF-kappa B inhibitor (abstract).

Khan et al. teach that inhibition of NF-kappaB modulates the COX pathway and this inhibition of NF kappa B can be therapeutically useful in diseases in which COXs are involved such as cancer, especially colorectal cancer (column 69).

One of ordinary skill in the art at the time of the invention would have found in prima facie obvious to employ the NF kappa B inhibitor, BAY 11-7085, taught by Izban et al. in patient suffering from colorectal cancer as a means for treatment of the disease. Such a person would have been motivated to do so because the prior art of Khan et al. clearly recognizes the contribution that a NF-kappa B inhibitor has in treating colorectal cancer. Further, the skilled artisan would have had a reasonable expectation of success in treating colorectal cancer because the inhibition of NF-kappa B, which is known to play a role in colorectal cancer, would have been treatable, or at least slowed by a known NF-kappa B inhibitor such as BAY 11-7085, taught by Izban et al.

With respect to claims, 9-15, 21, 26-28, it is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a

product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

With respect to claims 64-72, the determination of a dosage, mode of administration, addition or removal of pharmaceutically acceptable excipients and salts that have the optimum therapeutic index is well within the purview of one having ordinary skill in the art. Accordingly, the artisan would have been motivated to determine optimum pharmaceutically acceptable excipients in order to get maximum effect of the active agent. Moreover, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

With respect to the added limitation of an anchorage dependent cancer, one of ordinary skill in the art would have been motivated to administer the claimed compound to anchorage dependent cancer given that it is well known in the art that compound treats cancer.

*Applicant's Remarks*

Applicant alleges that the Examiner alleges that it would be obvious to use an NF-kappa B inhibitor are known to modulate COX, which is known to be involved in colorectal cancer and that this reasoning is fundamentally flawed (see page 7 of instant response). Further, Applicant alleges that the Examiner over generalizes the fact that NF-kappa B inhibitor regulates COX and incorrectly concludes that NF-kappa B inhibitors can be expected to have activity in diseases involving COX. Applicant alleges that Kahn teaches only of oligopeptides that inhibit NF-kappa B. Applicant provides 5 references, including Hu et al., Cory et al., Vega et al., Huerta-Yepez et al. and Mabuchi et al in order to show that BAY 11-7085 affects cancer cells through mechanisms besides COX (page 8 of instant response).

Finally, Applicant cites El-Rayes et al and Becerra et al and alleges that there is no evidence that COX inhibitors are effective in colorectal cancer.

*Response to Applicant's Arguments*

Applicant's traversal has been fully and carefully considered in their entirety, but failed to be persuasive.

Applicant's arguments seem to counter the evidence provided in Applicant's instant disclosure and further argues against the enablement of Applicant's own disclosure. Initially, it is noted that though Applicant provides 5 references to "show that BAY 11-7085 affects cancer cells through mechanisms besides COX" (page 8 of instant response), none of these references treat colon cancer cells, the instantly elected cancer. With regards to El-Rayes et al., the author teaches that COX-2 inhibitor does not display synergy or significantly improved results with two chemotherapeutic agents irinotecan and capecitabine, the author does not teach that the COX-2 inhibitor is ineffective for the treatment of colon cancer. The same is true for Becerra et al., which again does not teach that COX-2 inhibitor does not effectively treat colon cancer, but rather teaches that its addition with 5-fluorouracil and leucovorin does not seem to display synergy or significantly improved results.

Secondly, Applicant's instant disclosure is noted. Applicant discloses that the instantly disclosed NF-kappaB can be administered to cancer cells that express the COX-2 gene (page 14 of instant specification). COX-2 is commonly overexpressed in colorectal tumors and play roles in survival and metastasis in colorectal cancers. COX-2 overexpression plays a role in the susceptibility of the colon cancer cells to BAY 11-7085 induced apoptosis (page 67 of specification). Further, the re-adhesion of these floating cells causes a large and transient activation of NF-kappaB. This renders the adherent

cells exquisitely susceptible to NF-kappa B inhibitor induced apoptosis. The fact that the vast majority of transiently suspended HT-29 and DLD-1 cells which were allowed to readhere, became apoptotic following treatment with BAY 11-7082 or BAY 11-7085 indicated that NF-kappaB is an important survival factor for certain cancer cells such as colon cancer cells, during the process of re-adhesion, particularly cancer cells that express COX-2 (page 71 of specification). Given Applicant's own results and more importantly own conclusions, the Examiner is confused to Applicant's arguments that it has been incorrectly concluded that NF-kappa B inhibitor, such as the elected inhibitor, can be expected to have activity in diseases involving COX (see page 8 of instant response). Indeed, from Applicant's disclosure that COX-2 is not only involved in metastasis of colorectal cancers but additionally NF-kappaB inhibition would also lead to COX inhibition.

Applicant further states that it is not clear that the oligopeptides of Kahn et al actually affect COX and that COX activity can only be assumed. The Applicant has not provided any evidence as to these conclusions. The Examiner contends that NF kappa B modulates COX, column 69, as noted in the Office Action mailed on 5/29/2008.

### **Conclusion**

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/  
Supervisory Patent Examiner, Art Unit 1614



Application/Control Number: 10/505,244  
Art Unit: 1614

Page 8